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Claims 1-5 and 18-20 as amended below are directed to an allowable product. Pursuant to the procedures set forth in MPEP § 821.04(b), claims 6-17 as directed to processes of making or using the allowable product and previously withdrawn from consideration as a result of a restriction requirement, are hereby rejoined and fully examined for patentability under 37 CFR 1.104. Claims 6-17 as directed to processes of making or using the products of Groups I-V and VII-IX have NOT been rejoined.

Because a claimed invention previously withdrawn from consideration under 37 CFR 1.142 has been rejoined, **the restriction requirement between groups VI, XV, XXIV, XXXIII, and XLII as set forth in the Office action mailed on 8/6/09 is hereby withdrawn.** In view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer

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applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

An extension of time under 37 CFR 1.136(a) is required in order to make an examiner's amendment which places this application in condition for allowance. During a telephone conversation conducted on 2/23/11, Trupti Joshi requested an extension of time for 1 ADDITIONAL MONTH(S) (1 month previously paid for) and authorized the Director to charge Deposit Account No. 01-2300 the required fee of \$180 for this extension and authorized the following examiner's amendment. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

EXAMINER'S AMENDMENT

Replace claims 1 and 7 with the following:

Claim 1. An isolated protein comprising an amino acid sequence wherein:

a) the protein is able to bind coelenterazine and calcium, producing bioluminescence;

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b) the full-length amino acid sequence of the protein is identical by at least 90% to the full-length amino acid sequence of SEQ ID NO: 1 (Clytin) and;

c) the amino acid sequence of the protein comprises ~~one of the following single or multiple substitutions~~ a G₁₄₂→C substitution (the residue position being with reference to SEQ ID NO: 1) [[:]]

~~i) C₅₄→S;~~

~~ii) S₁₃₂→C;~~

~~iii) K₄₈→R, N₁₉₅→D;~~

~~iv) Q₆₈→R, A₉₀→V, T₁₈₄→I;~~

~~v) Y₈₂→F, K₁₁₀→N, F₁₂₅→L, S₁₄₉→R;~~

~~vi) G₁₄₂→C;~~

~~vii) I₅₃→V, S₁₄₉→R;~~

~~viii) N₁₈→D, I₄₀→V, K₅₆→R;~~

~~ix) Gly₅₈→Glu, Asp₆₉→Val, Ala₇₀→Cys, Lys₇₆→Arg, Lys₇₇→Gly,~~

~~Ile₇₈→Cys, Asp₈₁→Glu, Val₈₆→Ile, Glu₈₇→Ala, Ala₉₀→Gln,~~

~~Val₉₂→Leu, and Glu₉₇→Gln.~~

Claim 7. The polynucleotide of claim 6, having the sequence of SEQ ID NO: ~~11, 12, 13, 14, 15, 16, 17, 18, 19.~~

In claim 9, replace --A prokaryotic-- with --An isolated prokaryotic--.

Replace claims 10-12 with the following:

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Claim 10. A ~~mammalian~~-host cell according to claim 9
wherein the host cell is a mammalian cell.

Claim 11. ~~A method in vitro~~ An in vitro method for
detecting changes in intracellular calcium concentration, which
comprises:

a) providing a cell expressing ~~a photoprotein~~ the protein
according to claim 1;

b) allowing the protein to bind with coelenterazine to
constitute a photoprotein;

[[b)]] c) contacting the cell with an agent stimulating
calcium influx or calcium release from intracellular
stores; and

[[c)]] d) detecting the photoprotein bioluminescence.

Claim 12. A method of screening for compounds modulating
intracellular calcium concentration, which comprises:

a) providing a cell expressing ~~a photoprotein~~ the protein
of claim 1;

b) allowing the protein to bind with coelenterazine to
constitute a photoprotein;

[[b)]] c) contacting the cell with [[the]] a candidate
compound; and

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[[c)]] d) detecting the bioluminescence of the photoprotein.

In claim 13, replace --Amethod-- with --A method--.

Replace claim 20 with the following:

Claim 20. An isolated ~~photoprotein~~ composition comprising the protein of claim 1 and coelenterazine.

Cancel claims 4 and 15-17.

Claims 1-3, 5-14 and 18-20 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca E. Prouty whose telephone number is 571-272-0937. The examiner can normally be reached on Tuesday-Friday from 8 AM to 5 PM. The examiner can also be reached on alternate Mondays

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi, can be reached at (571) 272-0956. The fax phone number for this Group is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Rebecca Prouty/
Primary Examiner
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